EFFECTIVENESS, SAFETY AND TOLERABILITY OF BOTULINUM TOXIN IN FOCAL HYPERHIDROSIS & DYNAMIC FACIAL WRINKLES

This dissertation is submitted to

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

In partial fulfilment of the requirement of the award for the degreeof

M.D BRANCH XX

DERMATOLOGY, VENEREOLOGY AND LEPROSY

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DECLARATION

I solemnly declare that the dissertation titled, **Effectiveness, Safety and Tolerability of Botulinum toxin in Focal Hyperhidrosis and Dynamic Facial Wrinkles** was done by me at **Stanley Medical College and Hospital during 2010-2013** under the guidance and supervision of my **Chief Prof Dr. V. Anandan, M.D.**

The dissertation is submitted to **THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY** towards the partial fulfilment of requirement for the award of **M.D.Degree (Branch XX) in DERMATOLOGY, VENEREOLOGY & LEPRSOY.**

Place:

Date:

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CERTIFICATE

This is to certify that the dissertation titled**'EFFECTIVENESS, SAFETY AND TOLERABILITY OF BOTULINUM TOXIN IN FOCAL HYPERHIDROSIS & DYNAMIC FACIAL WRINKLES'**is submitted by**Dr.K.GOPALAKRISHNAN**to the**TheTamilnaduDr.M.G.R Medical University, Chennai** in partial fulfilment of the requirement of the award for the degree of **M.D BRANCH XX (DERMATOLOGY, VENEREOLOGY AND LEPROSY)**and is a bonafide work done by him under my direct supervision and guidance.

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CONTENTS

INTRODUCTION

BOTULINUM TOXIN IN DERMATOLOGY

Justinus Kernerfirst described botulinum toxin as a "sausage poison" and "fatty poison",[1] because the bacterium that produces the toxin often caused poisoning by growing in improperly prepared meat products. Kerner, a physician, first conceived a possible therapeutic use of botulinum toxin and coined the name botulism (from Latinbotulus - meaning "sausage").

In 1897, Emile van Ermengem found that the organism producing botulin toxin was a bacterium, which he named Clostridium botulinum.[2]

In 1928, P. Tessmer Snipe and Hermann Sommer were the first to purify the toxin.[3]

In 1949, Arnold Burgen's et al discovered, through an elegant experiment, that botulinum toxin blocks neuromuscular transmission by decreasingacetylcholine release.[4]

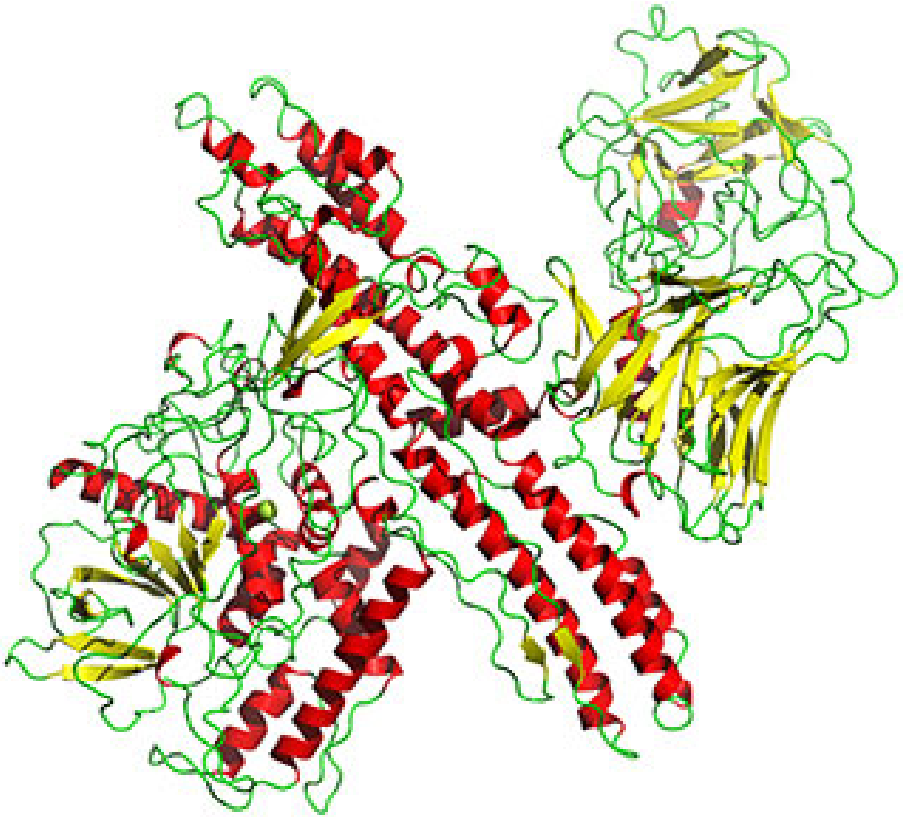
Botulinum finds several application in the field of dermatology as follows :

- Treatment of hyperhidrosis – axillary, palmar and plantar hyperhidrosis, gustatory sweating syndrome.

- Aesthetic dermatology – facial wrinkles.

- For skin tightening effect as is observed with meso-therapy

FIGURE 1 – 3D STRUCTURE OF BOTULINUM TOXIN



AIM OF THE STUDY

1. To study the effectiveness of botulinum toxin in palmar hyperhidrosis and dynamic facial wrinkles.

2. To analyse the safety and tolerability profile of it among the patients treated with it.

REVIEW OF LITERATURE

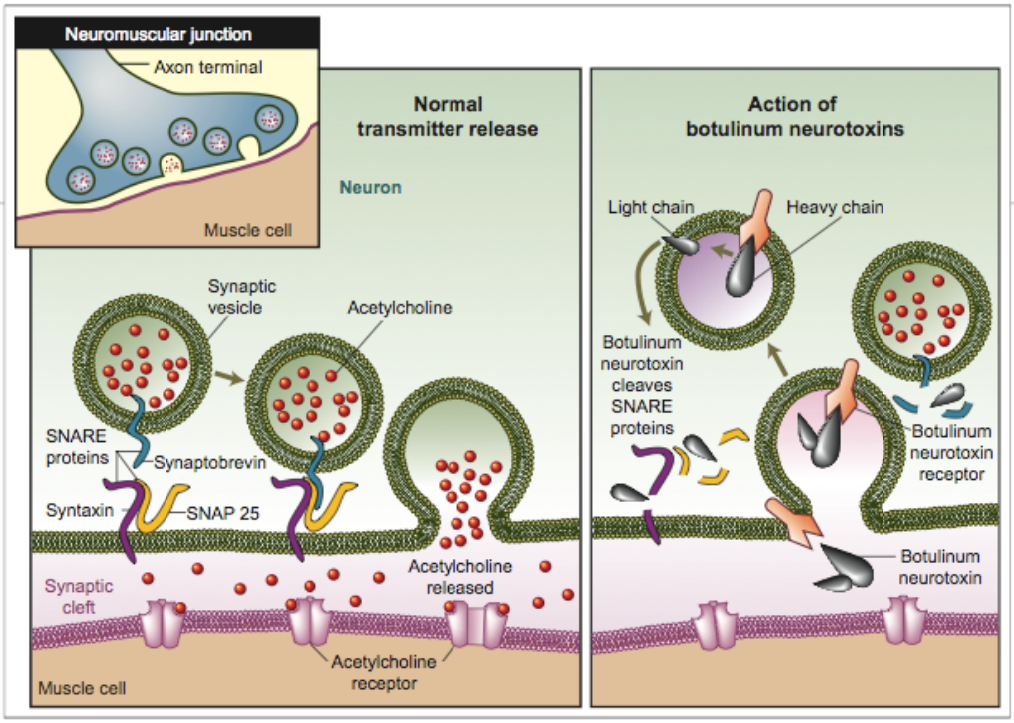
Various strains of the bacterium Clostridium botulinum produce, seven distinct serotypes of botulinum toxin (BTX) which includes A, B, C1, D, E, F and G all capable of affecting neural function [5]. Although all these serotypes produce chemical denervation resulting in atrophy of skeletal muscles by blocking acetylcholine (Ach) release from motor neurons at the neuromuscular junction (Fig. 2), they differ with regard to cellular mechanism of action and clinical profile [6].

BTX specifically inhibits acetylcholine release by cleaving proteins in the SNARE complex (required for Ach release)

BTX-Aacts by cleaving SNAP-25 (synaptosome associated protein), key protein for successful docking and release of Ach from vesicles within nerve endings.

BTX-B cleaves synaptobrevin or VAMP (vesicle associated membrane protein).

FIGURE 2 – MOA OF BOTULINUM TOXIN



BTX type A (BTX-A) was the serotype first developed for clinical use. **Neuronox®** (South Korea) is the brand available in India and used in this study.

Intramuscular injections of BTX-A have become the treatment of choice for a number of disorders characterized by muscular hyperactivity, such as strabismus[6], blepharospasm and hemifacial spasm[7], and cervical dystonia[8]. In addition, the ability of BTX to stop acetylcholine release from autonomic nerve endings supplying glandular tissue or smooth muscle has led to investigation of its use for other indications, including hyperhidrosis [9], migraine [10], tension headaches [11] and myofascial pain [12].

The only other available serotype is a formulation of **BTX type B** that was approved in the US by the Food and Drug Administration (FDA) in 2000 for the treatment of cervical dystonia, but has been used off-label to treat facial wrinkles and evaluated in several smaller clinical trials[15–17]. Research indicates that there are key differences in effects between BTX-A and BTX-B for the treatment of facial wrinkles - BTX-B has a more rapid onset of action but a shorter duration of effect, diffuses more widely, and is associated with greater pain and other side effects than BTX-A[18,19].

DILUTION AND HANDLING OF BOTULINUM TOXIN

Neuronox®is available as a lyophilised powder with approximately 50 U or 100 U per vial. The manufacturers recommend that the products be reconstituted with sterile, non-preserved saline. Data suggests that reconstitution with preserved saline may not alter the stability of BTX-A[20,21] and helps in considerable reduction of pain on injection[22]. For these reasons, preserved saline has become the reconstitution material of choice.

The optimum concentration of BTX for injections will depend upon the serotype, formulation and procedure. For cosmetic use of **Neuronox®**, the volume of diluent is 2.5 ml[20].Lower concentrations are useful for some indications, but if adverse effects due to spread of the toxin to unintended targets is a problem, increasing the concentration of toxin and decreasing the volume injected may prevent it. On the other hand, data suggest that amount of injection administered does not contribute to diffusion; in a dose-dilution study in which a total dose of 30 U was reconstituted in 1, 3, 5 or 10 ml, no differences in efficacy or safety were observed between groups[23].

Thepackage insert for **Neuronox®** suggests that the reconstituted toxin should be utilised within 4 hours, some physicians have reported using BTX-A 7 to 10 days after reconstitution with no observed alteration in potency[20], and Hexsel and colleagues found no significant differences in efficacy when injected within 6 weeks of reconstitution[25].The diluted vial is stored at 4°C . The diluted toxin is transferred to an insulin syringe with a 30-gauge needle is best for injecting it[26].

Dosing and Injection Schedules

The therapeutic effect of BTX-A injections is usually apparent within a day or two and are obvious for 3 or 4 months, although they may last for 6 months or longer. With repeated injections, there is a tendency for later injections to provide aesthetic improvement that lasts longer; it is possible that over the course of treatment, individuals change their habitual use of muscles that cause expression lines. Remodelling of the dermis and epidermis on a long-term basis helps to sustain the cosmetic effects also occurs in most individuals, because the tissue is no longer subjected to the same forces of muscle contraction.

Preoperative History and Conditions

Hyperkinetic lines result from the repeated contraction of muscles perpendicular to the wrinkles. Weakening or relaxing these muscles with BTX-A can smooth these lines, including horizontal lines on the forehead (from frontalis contraction), vertical lines in the glabellar region between the eyebrows (caused by the corrugator muscles), horizontal creases across the bridge of the nose (from procerus contraction), 'crow's feet' and lateral lines along the lower eyelid (caused by contraction of the lateral orbicularis oculi), and perioral lines (from contraction of the orbicularis oris). Deep grooves or folds elsewhere that are exacerbated by muscle activity are also amenable to treatment. Patients 30 to 50 years of age may be most responsive to BTX-A, because their wrinkles are more likely to be caused by muscle activity than by the loss of skin elasticity that occurs during aging.

CONTRAINDICATIONS

BTX-A therapy is contraindicated in the presence of neuromuscular disorders that could amplify the effect of the drug, such as myasthenia gravis or amyotrophic lateral sclerosis. Experience with BTX-A in pregnant and lactating women is lacking, and it is not a

recommended treatment in such individuals, although inadvertent use during pregnancy has not resulted in any reported teratogenicity or pregnancy issues[27]. The possibility of drug interactions exists, and patients taking aminoglycoside antibiotics should be administered lower doses of BTX-A. As is true for most injections, BTX-A should not be given in the presence of active infection at that site[28-35].

DESCRIPTION OF TECHNIQUES

Injections for aesthetic indications are given either intramuscularly, subcutaneously or intradermally . Intradermal injections are used especially in the Crow's feet area to minimize bruising. All of the usual precautions prior to any injection should be followed. The area may be chilled with ice before the injections to minimize any discomfort in sensitive individuals. Alternatively, a topical anesthetic can be applied 15 to 30 minutes prior to injection to minimize discomfort[35,39,45].

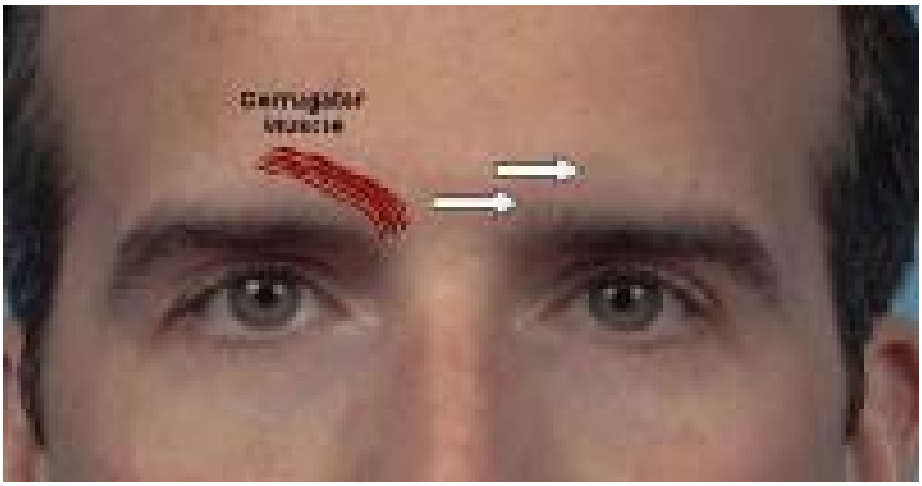
Electromyographic (EMG) guidance can be used to inject BTX into the most active region of the muscle. Once complete understanding of the relevant facial anatomy is attained, injection with an EMG system provides no advantage in using it. However, even experienced clinicians

may find EMG guidance to be useful for the occasional difficult-to-treat patient[39-42].

Glabellar Frown Lines

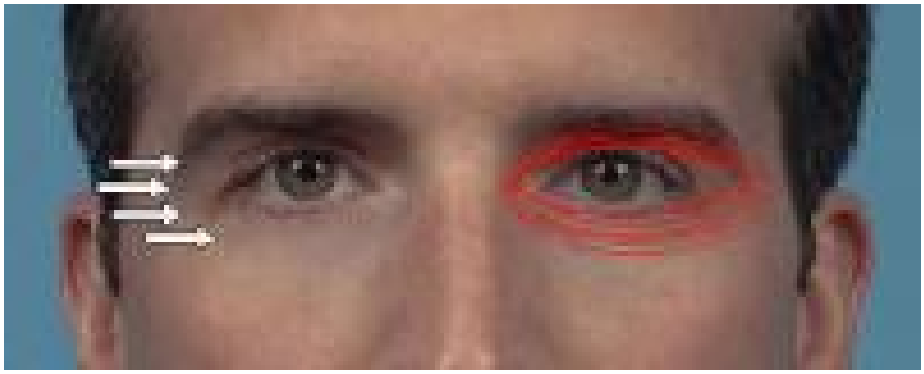
Frown lines in the glabellar region are caused by contraction of the corrugator supercilii and orbicularis oculi muscles, which pull the brow medially, and the procerus muscle and depressor supercilii, which pull the brow inferiorly. Because the corrugator and procerus are used only to control facial expression, the goal of treatment should be mainly to produce weakening of these muscles. The treatment sites and doses should be individualized because the anatomical location, size and use of the frown muscles vary greatly between individuals.

The patient is supine with the chin down position, insert the needle just above the superior bony orbital rim, directly above the inner canthus and inject an adequate dose–7 to 10 U in women and 15 to 20 U in men.The same procedure is done on the opposite side of the brow to ensure symmetry. Next , deliver 5 to 10 U into the procerus at the midline. The procedure effectively smoothes the glabellar lines at rest .



Crow's Feet

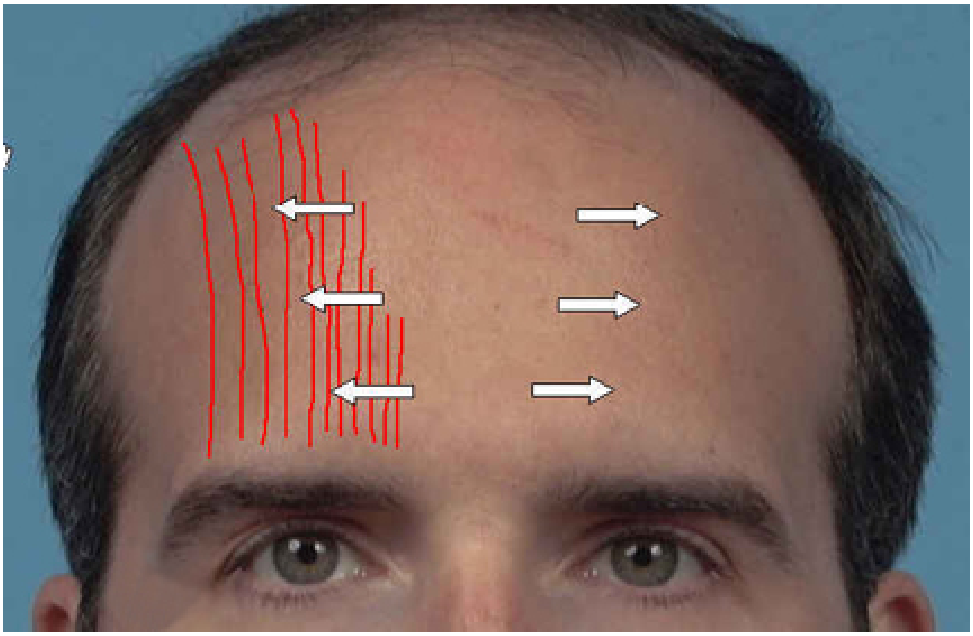
Contraction of the lateral fibers of the orbicularis oculi muscle produces ‘crow's feet', lines that radiate from the lateral canthus. Since tight closure of the eyelids requires orbicularis contraction, the goal of treatment is to produce weakening more in the lateral orbital area, rather than a complete paralysis of the muscle. Because the orbicularis oculi is richly innervated, multiple injections are required to weaken broad areas of the muscle.



Reported total doses for the treatment of crow's feet range from 8 to 16 U per side (in women) and 12 to 16 U per side (in men) distributed over multiple injection sites, with 3 to 4 U injected at a single site[27]. Injections are given when the patient is *not*smiling, or the toxin might affect the ipsilateralzygomaticus complex, causing upper lip ptosis. Injections are placed lateral to the lateral orbital rim, because more medial injections can result in a side effect of temporary lower eyelid droop. Care is taken to avoid injecting any superficial veins.

Horizontal Forehead Lines

Deep horizontal creases in the forehead are caused by the repeated contraction of the frontalis. This vertically oriented muscle is the brow elevator; it inserts superiorly into the galeaaponeurotica and inferiorly into the skin of the brow. Unfortunately, weakening the frontalis sufficiently to eliminate hyperkinetic forehead lines can result in undesired brow ptosis with a complete lack of expressiveness. Therefore, the goal of treatment is to only lessen, rather than completely eliminate, forehead lines. Ideally, the individual will still be able to elevate the eyebrows, albeit to a lesser extent, after treatment .



A wide ranges of dose and dilution have been prescribed for the treatment of horizontal forehead lines, but most reports emphasize that the injection sites should be kept above the brow to avoid ptosis[27]. A total of 10 to 15 U BTX-A is divided among multiple sites placed horizontally across the mid forehead, 2 to 3 cm above the eyebrows[47,52].

'Bunny Lines'

Contraction of the upper nasalis muscle results in fanning rhytides ('bunny lines') at the radix root of nose. BTX-A treatment weakens the upper nasalis effectively and dramatically soften it. Bunny lines are treated in conjunction withglabellar complex. Inject 2-4 units of BTX-A into each belly of the upper nasalis as it traverses the lateral bony dorsum

of the nose. Usually one injection per side is sufficient. The area is gently massaged following each injection to facilitate diffusion of the toxin; however, too-vigorous massage or massage in a downward direction could also result in lip ptosis.

Other wrinkles in face that could be treated with BTX-A include

1) **Repeated Nasal Flare** - Contraction of the nasalis muscle accentuates the nasal flare. Injection of 5 to 10 U of BTX-A bilaterally into the lower nasalisfibers covering the lateral nasal ala- the most active area of muscle contraction produces a good decrease in involuntary nostril flare.

2) **Nasolabial Folds in Selected Patients**

3) **Nasal Tip Droop** - Contraction of the depressor septinasi, a muscle located at the external base of the nasal septum, pulls the tip of the nose downward. Injection of 2 to 3 U of BTX-A into the depressor septi at the base of the columella, slightly elevates the nasal tip.

4) **Vertical Lip Rhytides (Perioral Lines)**

5) **Upper Gum Show** - The levatorlabiisuperiorisalaequenasi, muscle retracts the upper lip – chemo-denervation of the muscle with BTX-A, results in a moderate drop in the upper lip sufficient to cover the upper gum.

6) **Facial Asymmetry: Functional Muscle Imbalance -** Injections of BTX-A can also be used to correct facial asymmetry resulting from facial nerve palsies[40], dystonias[7,41], surgery[42] or trauma[43].

7) **Mouth Frown** - The Depressor angulioris(DAO)muscle pulls down the corner of the mouth in opposition to the zygomaticus major and minor muscles. BTX-A can be used to weaken the DAO resulting in resetting of muscular balance, allowing the zygomaticus to elevate the corners of the mouth and bring them to a horizontal position

8) **Melomental Folds (Marionette Lines)**

9) **Mental Crease**

10) **Peaud'Orange (Apple Dumpling) Chin**

11) **Masseteric Hypertrophy**

12) Horizontal Neck Lines

13) Platysmal Bands

14) Adjunctive Use - BTX-A is beneficial in many patients as an adjunct therapy to enhance or prolong the results of other cosmetic procedures. To chemodenervate specific muscles prior to surgery to can facilitate subsequent manipulation of tissues during the surgery and permit a better surgical correction or a better concealimg of the surgical incision. To decrease tension exerted on a wound or surgical incision by the underlying muscles, thereby promoting better healing with less scar formation. To prolong the effects of resurfacing[51] and many clinicians now use BTX-A injections along with their standard laser resurfacing protocol . Likewise, combination treatment with BTX-A and intense pulsed light (IPL) therapy may be a synergistic approach to the treatment of facial aging. BTX-A is also frequently used with soft tissue augmentation, where it prevents distortion of the filler and prolongs the beneficial effects of tissue augmentation .

POSTPROCEDURAL CARE

Manual pressure can be applied over the injection site immediately after withdrawal of the needle to prevent bruising. Depending upon the site of injection, the physician may massage the area after the injection to spread the toxin, but only if it is possible to do so without spreading the toxin to non-targeted muscles. To minimize undesired toxin diffusion, patients should be directed to remain upright for at least 2 to 4 hours after the procedure and to refrain from rubbing or manipulating the area for 24 hours. Because there is evidence suggesting that BTX-A binds preferentially at actively stimulated muscles, patients are asked to contract and relax the treated area as much as possible for 2 to 3 hours following the injections. Patients should be told to expect some transient redness, swelling or bruising at the injection sites, and patients should be advised that the effects of treatment will probably begin to diminish in 3 or 4 months.

COMPLICATIONS

BTX-A occasionally affects non-targeted muscles or glandular tissue in the areas surrounding the injection, which can result in effects such as eyelid drooping , lower eyelid laxness, epiphora (excessive

tearing), diplopia, brow ptosis, decreased strength of eye closure, dry eye, mouth incompetence, difficulties in speech and the inability to whistle. Use of careful injection technique to target the toxin to the appropriate muscles and the use of concentrated low doses to limit its diffusion to non-targeted muscles or glands are recommended to try to prevent the occurrence of these adverse effects. Generally, a higher concentration allows for more accurate placement, greater duration of effect, and fewer side effects, since lower concentrations may spread the toxin widely. Of note, there is an area of denervation at each point of injection of size about 1 to 1.5 cm (diameter, 2–3 cm) that is due to toxin spread

A quizzical or ‘cockeyed’ appearance can occur in the brow whenever the lateral fibers of the frontalis muscle have not been injected appropriately and these unparalyzed lateral fibers pull upward on the brow. Brow ptosis may last upto 3 months, while upper eyelid ptosis can persist from 2 to 12 weeks. Bruising, diplopia, ectropion, a drooping lower eyelid, and an asymmetric smile - caused by the spread of toxin to the zygomaticus major, are all reported complications of BTX-A injections in the periorbital area. Transient local bruising, ptosis, dry eyes, diplopia, and facial droop can occur with injections into the cheek.

Complications in the lower face involves effect on muscle function and facial expression, usually due to overenthusiastic use of BTX-A in large doses. Injections placed too close to the mouth, injection into the mental fold, and interaction with the orbicularis oris muscle can cause a flaccid cheek, incompetent mouth or asymmetric smile. Large doses (>100 U) of BTX-A, in the platysmaresulted in reports of dysphagia and weakness of the neck flexors.

Although one of the biggest concern with the use of BTX-A is the formation of neutralizing antibodies leading to non-response to subsequent injections, the overall risk is actually low (<5%) when BTX-A is used at usual doses for neurologic applications. Injecting the lowest possible effective doses, with the longest feasible intervals between injections, minimizes the chance for immunogenicity. Some believe that the total protein concentration is critical in determining potential immunogenicity; the protein content in currently available BTX-A is significantly lower than in previous batches and has been said to be less antigenic than the original product. Clinical experience with BTX-B is currently limited. However, although cross-reactive antibodies (to BTX-A and BTX-B) do occur, cross-resistance has not been a problem.

There is no long-term adverse effect reported, and no systemic safety problems have been found with FDA-approved uses of BTX-A.

FUTURE TRENDS

BTX-A has become the treatment of choice for smoothing hyperkinetic lines in the face and neck, creating a more pleasant and youthful appearance. Alone or in combination with surgery, soft-tissue augmentation, or ablative and non-ablative laser resurfacing, BTX-A treatment is both an art and a science, with its use in facial sculpting and enhancing, along with dermatologic correction. Moreover, the number of dermatologic indications for BTX-A is likely to continue to grow. Easy to use, minimally invasive, very well tolerated by patients and extremely safe, injections of BTX-A can be used alone or in combination with other cosmetic procedures and are an integral part of most cosmetic practices.

sHYPERHIDROSIS

Sweating is an essential thermoregulatory function. When the internal temperature rises, there are two main mechanisms to cool the body: radiative cooling due to cutaneous vasodilation and evaporative cooling due to sweat. Most sweat is produced by the eccrine sweat glands, and heat is dissipated as energy released by evaporation from the

skin surface. The designation ‘sweat’ has been applied to both the eccrine and apocrine glands, as well as to their secretory products, i.e. eccrine sweat and apocrine sweat . For the purposes of this discussion, the term ‘sweat’ applies to eccrine glands and their secretory products unless otherwise specified.

There are 2-5 million eccrine glands distributed within the skin of each individual. Only on the clitoris, glans penis, labia minora, external auditory canal and lips are they absent. The ductal orifices of the eccrine glands are visible only on the palms and soles, where, with 20- to 30-fold magnification, they can be seen along the dermatoglyphic ridges.

In healthy individuals, eccrine sweat is 99% water. The average adult can produce over 0.5 liters of sweat per hour, and trained athletes or those acclimatized to hot environments can produce up to 3-4 liters per hour[62]. Physically fit or acclimatized persons also initiate sweating earlier and conserve sodium, chloride and other electrolytes more efficiently than unconditioned individuals, resulting in cooling with minimal effect on water and electrolyte balance. Precision of thermoregulatory control is similar in men and women and diminishes only slightly with age[63].

Sweating is a reflex function that is primarily controlled through the sympathetic nervous system. These nerves are anatomically sympathetic but functionally cholinergic (i.e. acetylcholine, rather than norepinephrine, is the principal terminal neurotransmitter). Neural impulses for sweating (sudomotor impulses) travel from the anterior hypothalamus through the reticulospinal tracts to the appropriate level in the spinal cord, out through the rami communicantes to autonomic ganglia and then within sympathetic cholinergic neurons to the secretory cells of the eccrine glands. Adrenergic innervation has also been demonstrated for the eccrineglands, but it is not believed to be physiologically important[64]. In addition, the sweat glands, via a direct effect on the secretory cells, respond to certain drugs (e.g. cholinergic agonists) as well as to the local application of heat.

HYPERHIDROSIS

Hyperhidrosis is excessive production of sweat. The most widely used classification system divides it into primary and secondary types. Other classification systems separate hyperhidrosis into categories based on the source of the neural impulses that drive it: cortical (emotional), hypothalamic (thermoregulatory), medullary (gustatory), spinal cord and local axon reflexes.

Primary hyperhidrosis, the most common type, is characterized by excessive sweating localized to the palms, soles and/or axillae. It is stimulated by intense emotion or stress, and, in general, patients only have excessive sweating during waking hours. Primary hyperhidrosis is thought to arise from increased neural impulses from the cerebral cortex to the eccrine gland (hence the term 'cortical' hyperhidrosis). The glands themselves are normal in structure.

Secondary hyperhidrosis may be localized or generalized and is associated with medical conditions such as genetic syndromes, malignancy or infection.

Primary hyperhidrosis

Primary hyperhidrosis is defined as excessive sweating in localized areas (usually the palms, soles and/or axillae) that is not associated with a systemic disorder. Table 2.1 lists the diagnostic criteria[66]. Men and women of all races are equally affected. A family history can be elicited in 60-80% of patients with primary hyperhidrosis[67], with a pattern of inheritance suggesting autosomal dominant transmission with incomplete penetrance. Recently, a locus for primary palmar hyperhidrosis was mapped to chromosome 14q in three Japanese families[68].

Table 2.1

Criteria for the diagnosis of primary hyperhidrosis

CRITERIA FOR PRIMARY HYPERHIDROSIS
1. Focal, visible excess sweating **2.** Present for at least 6 months **3.** No apparent secondary causes **4.** At least 2 of the following: • Bilateral and symmetric • Impairs activities of daily life • At least 1 episode per week • Age of onset <25 years • Positive family history • Stops during sleep

Intense emotion or stress can elicit sweating in anyone. It occurs most often on the palms, soles or axillae and can also affect the face, especially the forehead and the cutaneous upper lip. The post-orgasmic sweating observed with sexual activity[69] may also derive from emotional stimulation.

Clinically significant primary hyperhidrosis occurs in two major forms, volar (palmoplantar) and axillary, which can coexist[62]. One of the two forms usually predominates as a problem in a given individual. The onset of volar hyperhidrosis is often during childhood, whereas axillary hyperhidrosis typically develops at or soon after puberty. Primary hyperhidrosis is seen in both cold and warm environments, but it is usually more problematic in hot weather. A chronic and unremitting course is characteristic, with little or no variation in association with age, disease or hormonal status.

Volar hyperhidrosis is the most common form of primary hyperhidrosis , affecting approximately 50-60% of patients[64,65]. The entire palm and sole, as well as the lateral aspects, tips and distal dorsal skin of the fingers, display sweating. Affected individuals are severely compromised socially and at work or school, with contamination of paper or work materials and embarrassment when shaking hands. As it begins

during childhood, it can cause self-conscious withdrawal from various social activities and sports.

Axillary hyperhidrosis is the second most common form of primary hyperhidrosis, affecting 30-50% of patients[65]. Affected individuals experience wet, stained clothing and unpleasant sweat trickling down the trunk. The right axilla usually produces more sweat than the left (60-40). Exceptionally, one axilla may be hyperhidrotic while the opposite axilla is hypohidrotic or virtually anhydrotic. These patients find work or social activities difficult to impossible. Odor (axillary bromhidrosis) is usually absent; the excessive quantities of eccrine sweat presumably wash away or dilute odorogenic apocrine sweat droplets and bacteria.

Secondary Hyperhidrosis

Secondary hyperhidrosis is caused and or associated with another systemic disorder. It can be localized to palmoplantar, axillary or other cutaneous sites or it may be generalized. There are many causes, which can be divided into categories based on the source of the neural impulse driving the response: cortical, hypothalamic, medullary, spinal or local.

Causes of cortical hyperhidrosis

CAUSES OF CORTICAL HYPERHIDROSIS
Primary hyperhidrosis
Secondary hyperhidrosis
Disorders of cornification
• **Palmoplantarkeratodermas** • **Pachyonychiacongenita** • **Congenital ichthyosiformerythroderma (bullous and non-bullous forms)**
Other genodermatoses
• **Epidermolysisbullosa: simplex >junctional** • **Dermatopathiapigmentosareticularis** • **Dyskeratosiscongenita** • **Pachydermoperiostosis (digital clubbing and thick, furrowed skin on the face and scalp)**

CAUSES OF CORTICAL HYPERHIDROSIS
• **Apert syndrome (craniosynostosis, digital anomalies, severe acne; FGFR2 mutations)** • **Nail–patella syndrome**
Hereditary sensory and autonomic neuropathies (HSANs)[‡]
• **Familial dysautonomia (Riley–Day syndrome; HSAN type III)** • **Congenital autonomic dysfunction with universal pain loss** • **Congenital sensory neuropathy (HSAN type II)**

Table 2.2

Drugs that can stimulate eccrine sweating

DRUGS THAT CAN STIMULATE ECCRINE SWEATING
Direct-acting cholinomimetic agents
• Acetylcholine • Anti-xerostomia drugs – Cevimeline – Pilocarpine • Methacholine
Cholinesterase inhibitors
• Anti-Alzheimer's drugs – Donepezil – Galantamine – Rivastigmine – Tacrine • Anticholinergic antidote – Physostigmine • Antimyasthenics – Ambenonium

DRUGS THAT CAN STIMULATE ECCRINE SWEATING
– Edrophonium (for diagnosis) – Neostigmine – Pyridostigmine

Adrenomimetic agents
• Dopamine • Epinephrine • Isoproterenol • Norepinephrine • Phenylpropanolamine
Antidiabetic (hypoglycemic) agents
• Insulins • Sulfonylureas
CNS stimulants
• Amphetamines • Caffeine • Theophylline

Antidepressants

- MAOIs
  - Isocarboxazid
  - Phenelzine
  - Selegiline
  - Tranylcypromine
- SSRIs
  - Duloxetine
  - Fluoxetine
  - Paroxetine
  - Sertraline
- Tricyclics
  - Amitriptyline
  - Amoxapine
  - Desipramine
  - Doxepin
  - Imipramine
  - Maprotiline
  - Nortriptyline

- Protriptyline
- Trimipramine

- Other
  - Buspirone
  - Trazodone

Antipsychotics

- Phenothiazines
  - Chlorpromazine
  - Fluphenazine
  - Perphenazine
  - Thioridazine
  - Trifluprom azine
- Other typical antipsychotics
  - Chlorprothixene
  - Haloperidol
  - Loxapine
  - Molindone
  - Thiothixene

Antipyretics
• Acetylsalicylic acid • NSAIDs
Opioids
• Fentanyl • Meperidine • Methadone
Other drugs
• Atomoxetine • Dextromethorphan • Ipecac • Pentoxifylline • Sibutramine • Sumatriptan • Tramadol • Yohimbine

Localized sweating can be observed in certain inflammatory skin disorders and at times in the skin immediately surrounding an intradermal injection site. Direct stimulation of a cutaneous sympathetic axon can induce sweating in an area approximately 4 cm in diameter[64]. The response is minimal and rarely noticed. Electrical and physical impulses as well as subcutaneous injection of drugs with nicotine-like effects on autonomic ganglia can incite this local form of hyperhidrosis. Presumably, mediators from inflammatory skin conditions (e.g. psoriasis, dermatitis) can also elicit localized hyperhidrosis. Substance P is believed to participate in the mediation of axon reflex sweating, and a number of other mediators, including kinins, dopamine, prostaglandins, angiotensin and adenine, may be involved[78].

Diagnosis of Hyperhidrosis

Key features
▪ Differentiation between primary and secondary hyperhidrosis is important
▪ Colorimetric and gravimetric methods document hyperhidrosis

The first step in the diagnosis of excessive sweating is to differentiate between primary and secondary hyperhidrosis. History will elicit location, duration and specific triggers. Other medical disorders and medications (including over-the-counter products) must be documented. An extensive review of systems should point to any secondary causes.

Patients with primary hyperhidrosis report excessive sweating of the volar and/or axillary areas triggered by stress, typically with an onset during childhood or adolescence. They usually have a positive family history and the review of systems is negative for secondary causes. Examination shows shiny, wet palms and soles or excessive sweat stains on clothing. These findings are sufficient to make the diagnosis .

Patients who do not fit the classic pattern of primary hyperhidrosis should undergo further evaluation with a directed history focused on possible etiologies and a complete physical examination. Laboratory testing and radiographic studies may be needed .

Table 2.3

Initial patient evaluation for secondary hyperhidrosis

INITIAL PATIENT EVALUATION FOR SECONDARY HYPERHIDROSIS	
Laboratory test	**Disease**
Serum electrolytes, BUN, creatinine	Renal disease (rare)
Blood glucose level	Diabetes mellitus
Thyroid function tests	Hyperthyroidism
Skin test for tuberculosis (e.g. PPD)	Tuberculosis
Chest X-ray	Tuberculosis, neoplasm
Complete blood count	Infection
Sedimentation rate	Infection, neoplasm, inflammatory disease
Antinuclear antibodies	Autoimmune connective tissue disease
Urinary catecholamines[*]	Pheochromocytoma

Further evaluation depends upon results .

[*] If suggestive signs or symptoms.

Measurement of sweat can be performed when such documentation is required. A grading scale for volar disease lists ‘low’ as a moist palm or sole without visible sweat droplets. ‘Moderate’ disease is characterized by sweating toward the finger tips. ‘Severe’ cases drip sweat. Axillary involvement can be measured by the sweat stains on clothing. A stain of <5 cm is considered normal; 5-10 cm, mild; 10-20 cm, moderate; and >20 cm, severe.

Colorimetric techniques such as the starch–iodine or quinizarinmethods[79] demonstrate the sweating pattern and will also reveal the location of the most active sweat glands in a given area. In the starch– iodine technique, iodine solution (e.g. 3.5% in alcohol) is applied to clean, shaved skin and allowed to dry, then starch powder (e.g. cornstarch) is brushed onto the area; the mixture turns blue–black in sites with sweating . A combination of paper impregnated with starch and iodine can also be utilized . Although not routinely performed in patients with hyperhidrosis, these tests can be used to plan treatment with botulinum toxin or local surgical ablation.

Additional quantitative assessment methods are available. In order to document amounts of sweat produced, gravimetric (via weighing filter paper before and after application to the skin) and evaporative (via a

device that assesses water vapor loss from the skin) measurements can be made in volar or axillary sites[79]. Most patients with axillary hyperhidrosis will produce at least 100-300 mg of sweat in a 5-minute test period with mental arithmetic as a sweating stimulus. Infrared thermography represents another method of evaluating sweat gland function, allowing comparison between anatomic areas and even individual glands.

Treatment of Hyperhidrosis

Key features
▪ Treatment options for hyperhidrosis include topical preparations, iontophoresis, oral anticholinergics or α-adrenergic blockers, biofeedback therapy, botulinum toxin and surgical procedures

Although over-the-counter antiperspirants are usually not strong enough to significantly improve the problem, more effective topical preparations are available; 20% aluminum chloride hexahydrate or 6.25% aluminum tetrachloride is usually the first-line treatment for localized hyperhidrosis. These solutions should be applied to dry surfaces at night, when sweating is diminished. Occlusion with gloves or plastic film

enhances penetration of the drug. Application is recommended for three to five consecutive nights, then one to two times a week as needed to control sweating. Treated skin can be washed the following morning. The salt precipitates in the sweat duct and blocks it. With chronic use, atrophy of secretory cells may be induced, and in some instances the entire eccrine unit degenerates. Burning and irritant contact dermatitis are common side effects, particularly in women who shave their axillae[23].

Table 2.4

Treatment of hyperhidrosis

TREATMENT OF HYPERHIDROSIS					
	Therapy	**Frequency**	**Side effects**	**Duration**	**Comments**
First-line	Topicals 20% aluminum chloride hexahydrate 6.25% aluminum tetrachloride Zirconium salts Aldehydes	Use nightly for 3–5 nights, then every few days as needed	Burning Irritant contact dermatitis	Days	Blocks sweat ducts Aldehydes not recommended due to sensitization
Second-line	Iontophoresis	2–3 times a week	Discomfort during procedure	Days	Blocks sweat ducts
	Botulinum toxin A	Every 4–6 months	Discomfort during injection Weakness of underlying muscles	Months	Prevents release of acetylcholine

TREATMENT OF HYPERHIDROSIS					
	Therapy	**Frequency**	**Side effects**	**Duration**	**Comments**
	Oral therapy	As needed		Hours	
	Oxybutynin Glycopyrrolate	1.25–5 mg bid 1–2 mg bid	Dry mouth and urinary retention most common; also confusion and decreased mental status		Anticholinergic Anticholinergic
	Clonidine	0.1–0.3 mg bid	Hypotension, rebound hypertension		α_2-Adrenergic agonist
	Clonazepam	0.25–0.5 mg bid	Sedation		Anxiolytic
Third-line	Local excision	Once	Scarring	Permanent	Last resort
	Sympathectomy		Compensatory hyperhidrosis Horner's syndrome	Usually permanent	

Some patients who sweat significantly at night require a preliminary dose of an anticholinergic (glycopyrrolate 1 mg or propantheline bromide 15 mg) 1 hour before application for the first few applications. This reduces sweating enough to prevent washing away of the topical solution. Other topical preparations include zirconium salts, which may be effective in the axillae but are generally not helpful on volar skin. Topical aldehyde agents such as formaldehyde and glutaraldehyde are effective, especially for volar disease. However, they have been abandoned due to frequent allergic sensitization that can result in cross-reactions with aldehydes in the environment (e.g. in lotions, soaps, shoes). Other side effects include discoloration of the skin.

Tap water iontophoresis over 20 minutes two to three times a week may be helpful. The mechanism of action is unknown but is believed to relate to blockage of the eccrine duct within acrosyringium. Side effects are minimal and include tingling of the skin during treatment. Introduction of anticholinergic medications via iontophoresis is not advised, owing to systemic absorption and unacceptable side effects.

Oral anticholinergics will decrease sweating in most patients. The most commonly used agents are oxybutynin[80] and glycopyrrolate[81]. Unfortunately, high doses are often required to control the hyperhidrosis

and unacceptable side effects frequently occur at these doses, including dry eyes, dry mouth, insomnia, mental status changes (e.g. confusion, hallucinations), palpitations, seizures, blurred vision, bowel disturbances, urinary retention and hypertension.

Clonidine (an α_2-adrenergic agonist that decreases central sympathetic outflow) and phenoxybenzamine (an α-adrenergic blocker) have been used with some success in anecdotal reports[82,83]. Potential side effects include hypotension, rebound hypertension, sedation, constipation, weakness and headache.

Botulinum toxin type A (BTX-A) has been approved by the Food and Drug Administration in the US for the treatment of axillary hyperhidrosis; it is also effective for volar disease. BTX-A works by preventing release of acetylcholine from cholinergic neurons . Injection into hyperhidrotic skin will produce near anhidrosis for 4 to 6 months. Side effects, if any, are short-lived. Pain during injection is the most common complaint–when given in volar sites, a regional nerve block is usually performed prior to the procedure. Topical anesthetics are typically sufficient for the axilla. Muscle weakness, especially of the intrinsic muscles of the hands or feet, may occur and resolves spontaneously over 2 to 5 weeks. Compensatory hyperhidrosis has not been observed[84].

Surgical treatment represents the final option after other therapeutic modalities have failed. Excision of the sweat glands is often effective for axillary disease, but radical resection of the entire axillary skin causes significant scarring. Compensatory hyperhidrosis is not seen with this form of local surgery. Newer methods include removal or destruction of the axillary sweat gland layer by surgical dissection, curettage or liposuction[84,].

Although sympathectomy is the last resort for patients with volar hyperhidrosis, advances in endoscopic surgery have decreased the morbidity associated with this procedure. Sympathectomy at the T2–T3 level for palmar disease and the lumbar area for plantar disease is effective. Risks of the procedure include Horner's syndrome, hypotension and pneumothorax. Compensatory hyperhidrosis of the trunk or gustatory facial sweating may occur[23] and the hyperhidrosis may gradually recur.

MATERIALS AND METHODS

STUDY DESIGN

Type of study: Prospective non-randomized interventional study.

Place of study: Department of Dermatology,
Government Stanley Medical College, Chennai

Study period : May 2011 to October 2012 (18 months)
First 6 months: Interventional period
Next 12 months: Follow-up period

Sample size: 30patients of both sexes; age group: 15 to 75 years
20 patients with palmoplantar hyperhidrosis
10 patients with horizontal frontal line or crow's feet.

The patients enrolled for the study were pooled from those attending the Dermatology out patient department. Initially , 30 patients with palmoplantar hyperhidrosis who came with complaints of excessive sweating of palms and soles ; 20 patients with facial wrinkles were subjected to the pre-procedure consultation, assessment and investigations as given below. Out of them , 20 patients with

palmoplantar hyperhidrosis, 7 patients with Crow's feet , 3 patients with horizontal frontal lines were enrolled according to the inclusion and exclusion criteria. The mean age group was years of both sexes.

PRE- PROCEDURE CONSULTATION

- Thorough explanation of the procedure , course of treatment and potential adverse effects were explained
- Informed and written consent were obtained
- A thorough history regarding the onset , duration, etiological factors, complications, other systemic illness , hypersensitivity to any drugs, pregnancy, lactation and past history regarding any modes of treatment for the condition was taken. (ANNEXURE-I)

PRE- PROCEDURE ASSESSMENT

A meticulous examination as given in ANNEXURE –I was done with the following assessments

- Minors starch iodine test
- Hyperhidrosis severity scoring scale
- Photographic recording

Investigations

In all the patients bleeding time and clotting time was measured.

With the history. Clinical examination and the aid of laboratory investigations, patients were selected according to the inclusion and exclusion criteria.

Inclusion criteria

1) Age 15 – 70 years.

2) Sex – both Male & Female

3) Willing to be enrolled for the complete study period

4) Patients not responding to medical management

Exclusion criteria

1) Patient with neuromuscular disorders.

2) Pregnancy

3) Lactation.

4) Patients receiving drugs with neuromuscular blocking properties like amino glycosides, spectinomycin in the previous 3 days.

5) Patients with known hypersensitivity to BTX-A.

Procedure

Requirements

- Botulinum toxin A vial – 100 units (NEURONOX)
- 0.9% saline as diluent
- Insulin syringes
- Gloves
- Alcohol swabs
- Sterile gauze
- Ice packs
- Topical anaesthetic (EMLA)

Technique

Preparation of injection

The BTX-A containing vial is diluted with 2.5ml of normal saline and gently rolled between fingers to get a clear solution. The diluted solution is withdrawn into insulin syringes the volume in each according to convenience. The dosage calculation is 1 unit marking in syringe corresponds to 1 unit of BTX-A.

Positioning of patient

Patient is in recumbent position for comfort and convenience.

Preparing the patient

Intradermal test for BTX-A is given over volar aspect of left forearm.

Anaesthesia – topical anaesthetic (EMLA) is applied over the injection sites under occlusion until adequate anaesthesia is achieved.

The skin where the injection is to be given is wiped with surgical spirit.

Hyperhidrosis – the dominant hand of the patient is chosen for injection with the other kept as control.

Facial wrinkles – both sides are treated with injection sites marked with skin marking pencil.

Injection of BTX-A

Hyperhidrosis – the palm is divided into squares of area 2 cm^2 and 2 units of BTX-A is injected intradermally into the centre of each square. In the palmar aspect of fingers 2 units is injected into the centre of each phalanx.

Wrinkles –

Forehead lines – two rows of equally spaced points which are 2 cm apart are marked on the forehead as shown in the pictures. The lower row should be at least 1 cm above the brow and the inter-row distance should be 2 cm.

Crow's feet – 3 injection sites on each side are marked ; the first 1cm away from the bony margin from lateral canthi ; two other points 1 cm above and below the first point and just medial to it are marked a as shown in the pictures.

Immediately after the procedure ice packs are placed over the injection sites for 3 – 5 minutes.

Post procedure advice

To avoid lying down for 4 hours in patients treated for wrinkles.

To avoid any rigorous activity of the injected hand .

Follow up

Hyperhidrosis: 1st day, 10th day, 4^{th} week, 8^{th} week, 16^{th} week and 24^{th} week and once in 3 months after that.

At each visit minors starch iodine test and severity assessment using scoring system were done.

Wrinkles: 1^{st} day, 10^{th} day, every 4 weeks thereafter

At each visit photographic assessment was done.

HYPERHIDROSIS DISEASE SEVERITY SCORE	
1	Sweating is not noticeable and never interfere with daily activities
2	Sweating is tolerable but sometimes interferes with daily activities.
3	Sweating is barely tolerable and frequently interferes with daily activities.
4	Sweating is intolerable and always interfers with daily activities

Response rate

In both hyperhidrosis and wrinkles maximal response to treatment is recorded on the 10^{th} day after treatment and the response were assessed using the following criteria

Hyperhidrosis

Complete response – more than 75% reduction in sweating with severity score of l.

Partial response – between 35% to 75% reduction in sweating with severity score of 2.

No response – less than 35% reduction in sweating with severity score of 3 and above.

Wrinkles

Complete response – more than 75% reduction in visible wrinkles.

Partial response – between 35% to 75% reduction in visible wrinkles.

No response –no significant reduction in visible wrinkles.

RELAPSE RATE

In both the conditions relapse was taken as complete recurrence of symptoms similar to that before treatment.

RESULTS

Total no. of patients in the study : 30

The sex distribution of the patients included in the study

Male	7
Female	21

The age wise distribution of patients

15 – 35	20
36 – 55	8
56- 75	2

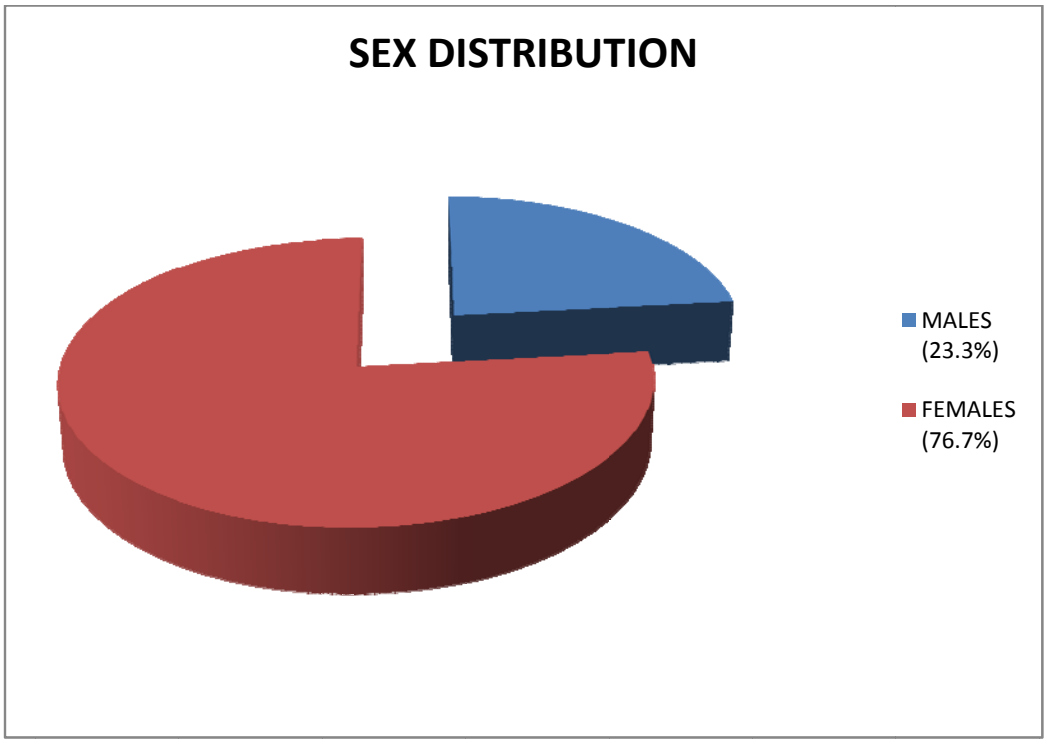
The average age of the patients in the study group : 35.5

THE RESPONSE RATE

	HYPERHIDROSIS	**WRINKLES**
Complete response	18/20(90%)	7/10(70%)
Partial response	2/20(10%)	3/10(30%)

THE RECURRENCE RATE

	4th week	**8th week**	**16th week**	**24th week**
Relapse rate for hyperhidrosis	2/20(10%)	3/20(15%)	5/20(25%)	16/20(80%)
Relapse rate for wrinkles	1/10(10%)	2/10(20%)	4/10(40%)	6/10(60%)


SEX DISTRIBUTION
MALES (23.3%)
FEMALES (76.7%)

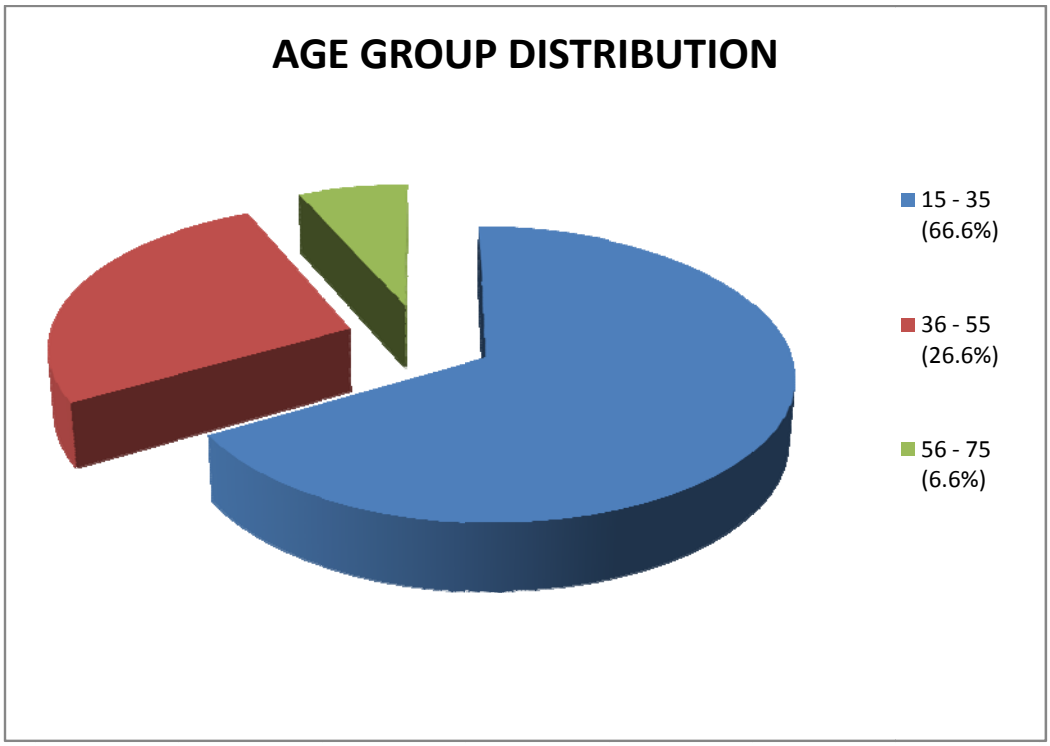

AGE GROUP DISTRIBUTION
15 - 35 (66.6%)
36 - 55 (26.6%)
56 - 75 (6.6%)

CHART SHOWING RESPONSE RATE AT 10th DAY POST TREATMENT

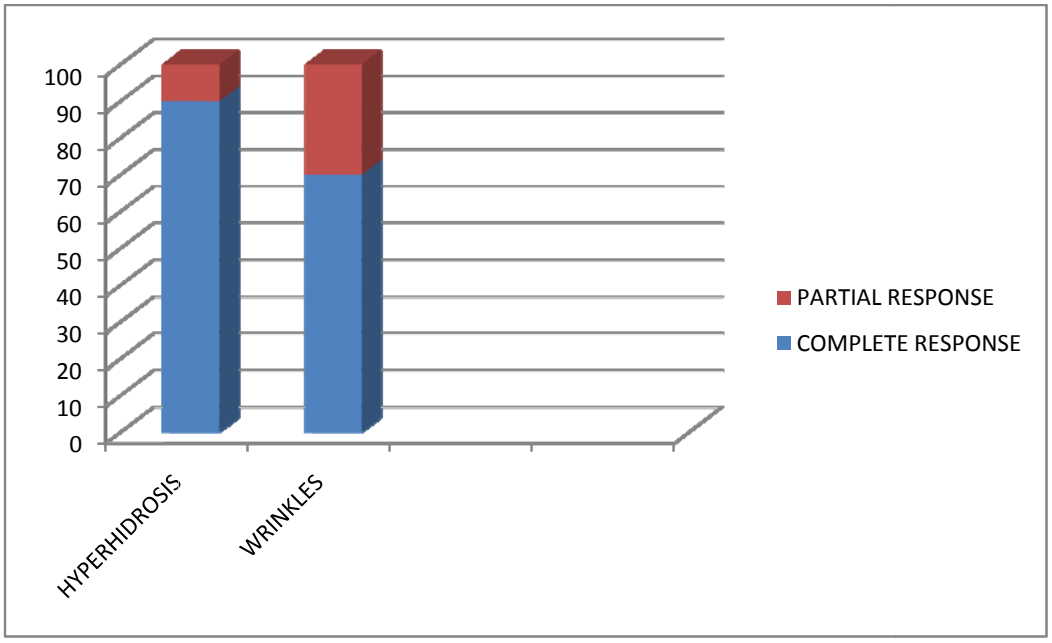
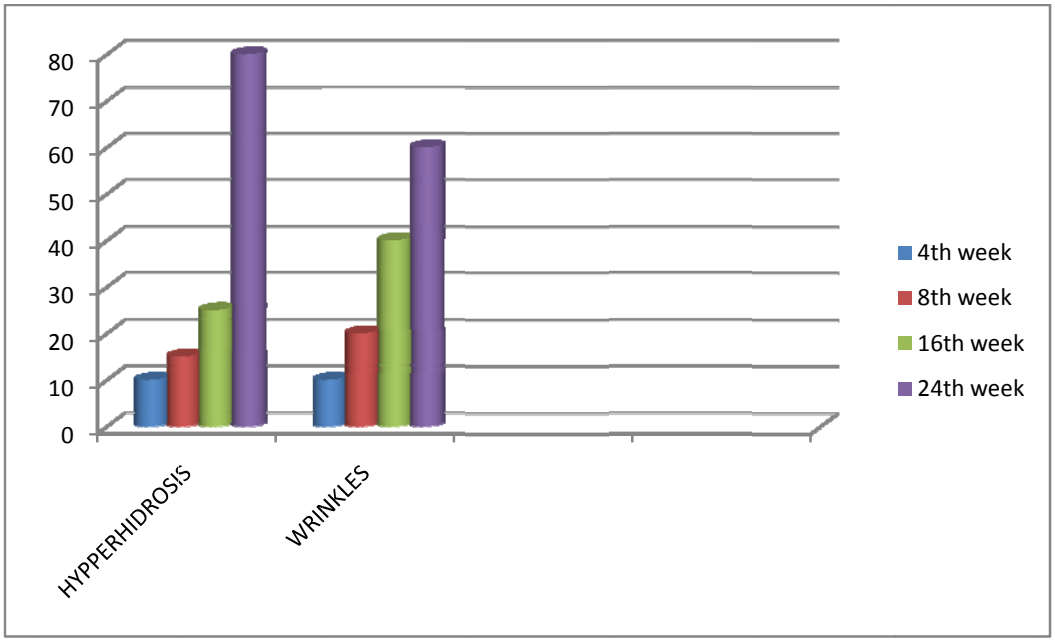


CHART DEPICTING THE RELAPSE RATE AS NOTICED DURING FOLLOW-UP



Interpretation of results

- BTX-A is in effective in both hyperhidrosis and wrinkles with most patients having complete response.

- The duration of the response maintained has inter-patient variability with an average of 14 weeks.

COMPLICATIONS OBSERVED

- The following complications were noted in the study

COMPLICATIONS	NO.OF PATIENTS
Pain over the treated site	3
Hematoma over the site	2
Hand muscle weakness	3

- No immediate complications like hypersensitivity , were noted.

- No serious complication like ptosis were noted.

DISCUSSION

Hyperhidrosis

Several medical managements are available for focal hyperhidrosis in the form of Topical antiperspirants like 1% formalin and aluminium chloride solutions. The disadvantage with these agents are that their mean duration of action is roughly few hours so they have to be applied on a daily basis resulting in poor patient compliance.

Oral agents like anticholinergic, beta blockers are sought with significant systemic side effects.

Iontophoresis requires minimum of thrice weekly to daily sittings depending upon the response which roughly lasts from few hours to few days. Few patients might be resistant to all the above modalities of treatment.

Botulinum toxin

In anearlier study done by Solomon and Hayman, 20 subjects having recalcitrant palmar and digital hyperhidrosis were treated with botulinum toxin type A , 50 - 65 U in one hand. Treatment reduced sweat production significantly in the treated areas, with effect lasting from 4 to

9 months, although reduced sweating persisted in all patients for the 12-month evaluation period.

Another study by Bodokh and Branger compared the effectiveness of BTX-A given in one hand compared with no treatment in the other control hand. Assessments included subjective and objective measurements, using gravimetric scales and Minor's iodine starch test. This study showed a significant improvement in 15/20 (75%) patients treated for palmar hyperhidrosis, with no serious adverse events . (Evidence levels: IIa, III)

It has been expressed that botulinum toxin type A injections in the palm may impede the release of acetylcholine at the neuromuscular junctions, thereby decreasing muscle tone and function in the hand; however, this has not been found to be true (Evidence level: IIb). Lowe *et al*. investigated the effectiveness of BTX-A vs. placebo in the treatment of palmar hyperhidrosis in 19 patients and concluded that patients experienced a significant improvement in palmar hyperhidrosis without a concomitant decrease in grip strength, finger dexterity, or the occurrence of any adverse events (Evidence level: Ib).

Our study results correlated well with the above studies in that all patients treated had good response which lasted for an average of 14 weeks with no serious adverse events though transient hand weakness were noted in 50% of those treated.

Pain during injection can be addressed through application of ice packs, use of the Dermojet delivery system or anesthetic procedures

Wrinkles

The cosmetic awareness in our society has recently witnessed a sea change with more number of people, both men and women giving significant importance to aesthetics in day to day life. The appearance of the skin in particular that of the face in terms of colour, texture and smoothness has gained undue social significance and the dissatisfaction with it can result in significant social morbidity, withdrawal, low self-esteem and so on. People are willing to undergo aesthetic procedures despite the cost. In this background botulinum toxin has gained importance both as a monotherapy and as an adjunct to several other aesthetic procedures. In the treatment of facial wrinkles, botulinum toxin A has been found to effective and has received FDA approval for the treatment of upper face. The dermatologist of this era is bound to have

adequate knowledge, experience and expertise of this unique treatment modality.

Many studies done by Blitzer et al and Pribitkin et al have shown the effectiveness of botulinum injections for hyper functional lines.These studies confer certain characteristics of successfully treated patients. The ideal patients are the ones with thin skin, fine wrinkles, lines that are exacerbated by muscle contraction, and hyperfunctional lines that can be spread out with their fingers. Blitzer et al described a "glabellar-spread test" in which the physician is able to spread out the hyperfunctionalglabellar lines to project the maximum benefit that a paralytic injection could achieve.

Carruthers et al, in a consensus panel article, stated that panel members agreed that preserved saline could also be used.An insulin syringe with a 30-gauge needle works nicely for injection. The insulin syringe does not waste any of the solution in the hub of the syringe. Some clinicians are moving to 32-gauge needles, which has better patient tolerance.

Indication/Scenario for Reinjection

If a patient feels dissatisfied with the original injection, reinjection can be performed 1 week post-injection. However, 2-3 weeks after the first injection is probably a more practical time for a return clinic visit. Normally , 2.5-5 U are used for reinjection. Reinjection strategies are yet to evolve. If the patient has a satisfactory result with reinjection, the next visit is at 2-3 months or when the patient requests another treatment.

Complications

The most dreaded complication is temporary paralysis of nearby facial musculature. Nearly 1-3% of patients may experience a temporary upper lid or brow ptosis; the most serious complication to the patient is upper lid ptosis. This results when there is migration of the botulinum toxin to the levatorpalpebraesuperiorismuscle. The ptosis usually persist for 2-6 weeks. It can be treated with topicalapraclonidine. This is an alpha-adrenergic agent that stimulates the Müller muscle and immediately elevates the upper eyelid. This treatment can usually raise the eyelid 1-3 mm. Treatment with1-2 drops 3 times per day continues until the ptosis resolves.

Bruising usually occurs if a small vein is lacerated or a patient is on aspirin, vitamin E, or NSAIDs. Strictly , patients should stop taking these products 2 weeks before the procedure. Headaches can occur after injections; however, in one study done by Carruthers et al, this did not exceed the placebo group.[6]This is due to the trauma of the injection and not something inherent in the toxin. In fact, botulinum toxin injections are quite safe. To date, no significant long-term complication ofbotulinum toxin injections has been identified

Future

The popularity of BTX is incredible in the field of cosmetic surgery. The use and scope of botulinum toxin increases every year. Patients have shown a very high degree of satisfaction with this procedure. Current research focuses on using BTX as an adjunct therapy to a myriad of surgical and ablative procedures.

Botulinum toxin A has been used in significant numbers for the past 20 years. It has proved to be an extremely safe strategy for selectively inducing muscle paralysis.

CONCLUSION

The following are the conclusions derived from this study

- Botox is a valuable treatment for both hyperhidrosis and facial wrinkles.

- Botox is effective in a single sitting. No other treatment modality for hyperhidrosis is effective in a single sitting.

- The results of this study show that complete response to botox was seen in 18/20(90%) and partial response in 2/20(10%) patients treated for hyperhidrosis.

- Complete response was seen in 7/10(70%) and partial response in 3/10(30%) in those treated for wrinkles.

- The recurrence rate was 16/20(80%) and 6/10(60%) in hyperhidrosis and wrinkles respectively at the end of 24 weeks.

- Only minor side effects like pain after injection, hematoma, and mild hand muscle weakness were noted.

- No major complications like anaphylaxis, ptosis, paralysis of facial or hand muscles were observed.

- The cost involved may be a factor and therefore this treatment should offered to patients with hyperhidrosis when

Not responding to other modalities of treatment.

A quick response is needed ahead of socially important situations like an examination, marriages etc.

- Hence BTX is a safe, in-office procedure which can be performed without hospitalisation when done by a well-trained dermatologist with expertise.

BIBILIOGRAPHY

1) Frank J. Erbguth (2004). "Historical notes on botulism, Clostridium botulinum, botulinum toxin, and the idea of the therapeutic use of the toxin". Movement Disorders (John Wiley & Sons, on behalf of the Movement Disorder Society) 19 (S8): S2–S6. doi:12.1002/mds.20003. PMID15027048.

2) vanErmengem, E.P. (February 1898). "Uebereinenneuenanaëroben Bacillus und seine BeziehungenzumBotulismus" (in German). Zeitschriftfür Hygiene und Infektionskrankheiten26 (1): 1–56. doi:10.1007/BF02220526. PMID399378.

3) Snipe, P. Tessmer&Sommer, H. (August 1928). "Studies on Botulinus Toxin, 3. Acid Precipitation of Botulinus Toxin". The Journal of Infectious Diseases, (University of Chicago Press) 43 (2): 152–160. doi:10.1093/infdis/43.2.152. ISSN0022-1899. JSTOR30083772.

4) A. S. V. Burgen, F. Dickens, and L. J. Zatman (August 1949). "The action of botulinum toxin, on the neuro-muscular junction". The Journal of Physiology (University of Chicago Press) 109 (1–2):

10–24. PMC1392572. PMID15394302. http://www.jphysiol.org/cgi/pmidlookup?view=long&pmid=15394302.

5) In: Jankovic J, Hallett M, ed,Therapy with Botulinum Toxin, New York: Marcel Dekker; 1994.

6) Eleopra R, Tugnoli V, Rossetto O, et al: Different time courses of recovery, after poisoning with botulinum neurotoxin serotypes A and E in humans. NeurosciLett 1998; 256:135-138.

7) Scott AB: Botulinum toxin injection, into extraocular muscles as an alternative to strabismus surgery,Ophthalmology 1980; 87:1044-1049.

8) Carruthers J, Stubbs HA: Botulinum toxin for benign essential blepharospasm, hemifacial spasm and age-related lower eyelid ectropion,Can J NeurolSci 1987; 14:42-45.

9) Jankovic J, Schwartz K: Botulinum toxin injections, for cervical dystonia. Neurology 1990; 40:277-280.

10) Glogau R: Botulinum A neurotoxin for axillary hyperhidrosis ,No sweat Botox. DermatolSurg 1998; 24:817-819.

11) Silberstein S, Mathew N, Saper J, et al: Botulinum toxin type A, a migraine preventive treatment. Headache 2000; 40:445-450.

12) Blumenfeld A: Botulinum toxin type A, an effective prophylactic treatment in primary headache disorders. Headache 2003; 43:853-860.

13) Porta M: A comparative trial of botulinum toxin type A , methylprednisolone for the treatment of myofascial pain syndrome and pain from chronic muscle spasm. Pain 2000; 85:101-105.

14) Ranoux D, Gury C, Fondarai J, Mas JL, Zuber M: Respective potencies of Botox and Dysport: a double blind, randomised, crossover study in cervical dystonia.,JNeurolNeurosurg Psychiatry 2002; 72:459-462.

15) Simonetta Moreau M, Cauhepe C, Magues JP, Senard JM: A double-blind, randomized, comparative study of DysportvsBotoxin primary palmar hyperhidrosis,Br J Dermatol 2003; 149:1041-1045.

16) Ramirez AL, Reeck J, Maas CS: Botulinum toxin type B, (Myobloc) in the management of hyperkinetic facial lines. Otolaryngol Head Neck Surg 2002; 126:459-467.

17) Alster TS, Lupton JR: Botulinum toxin type B, for dynamic glabellarrhytides refractory to botulinum toxin type A,DermatolSurg 2003; 29:516-518.

18) Sadick NS: Prospective open-label study of botulinum toxin type B (Myobloc), at doses of 2,400 and 3,000 U for the treatment of glabellarwrinkles,DermatolSurg 2003; 29:501-507.

19) Lowe N, Lask G, Yamauchi P. Efficacy and safety of botulinum toxins A and B, for the reduction of glabellarrhytids in female subjects, Presented at the American Academy of Dermatology 2002 Winter Meeting; 2002 February 22-27; New Orleans, LA.

20) Matarasso SL: Comparison of botulinum toxin types A and B, a bilateral and double-blind randomized evaluation in the treatment of canthalrhytides. DermatolSurg 2003; 29:7-13.

21) Klein AW: Dilution and storage of botulinumtoxin,DermatolSurg 1998; 24:1179-1180.

22) Huang W, Foster JA, Rogachefsky AS, Pharmacology of botulinum toxin. J Am AcadDermatol 2000; 43:249-259.

23) Alam M, Dover JS, Arndt KA, Pain associated with injection of botulinumA exotoxin reconstituted using isotonic sodium chloride with and without preservative: a double-blind, randomized controlled trial. Arch Dermatol 2002; 138:510-514.

24) Carruthers A, Carruthers J Dose dilution and duration of effect of botulinum toxin type A (BTX-A) for the treatment of glabellarrhytids, Presented at the American Academy of Dermatology 2002 Winter Meeting; 2002 February 22-27; New Orleans, LA.

25) Lowe NJ: Botulinum toxin type A for facial rejuvenation: United States and United Kingdom perspectives,DermatolSurg 1998; 24:1216-1218.

26) Hexsel DM, Trindade de Almeida A, Rutowitsch M, et al: Multicenter, double-blind study of the efficacy of injections with botulinum toxin type A reconstituted up to six consecutive weeks before application,DermatolSurg 2003; 29:523-529.

27) Flynn TC, Carruthers JA, Carruthers JDA: The use of the Ultra-Fine II short needle 0.3-cc insulin syringe for botulinum toxin injections,J Am AcadDermatol 2002; 46:931-933.

28) Carruthers J, Fagien S, Botox Consensus Group : Consensus recommendations on the use of botulinum toxin type A in facial aesthetics. PlastReconstrSurg 2004; 114(suppl):1S-22S.

29) Smith KC, Comite SL, Balasubramanian S, Carver A, Liu JF,Vibrationanesthesia: a noninvasive method of reducing discomfort prior to dermatologic procedures,Dermatol Online J 2004; 10:1.

30) Carruthers JA, Lowe NJ, Menter MA, et al: A multicenter, double-blind, randomized, placebo-controlled study of efficacy and safety of botulinum toxin type A, in the treatment of glabellarlines,J Am AcadDermatol 2002; 46:840-849.

31) Carruthers JD, Lowe NJ, Menter MA, et al: Double-blind, placebo-controlled study of the safety and efficacy of botulinum toxin type A, for patients with glabellar lines. PlastRecontrSurg 2003; 112:1089-1098.

32) Carruthers A, Carruthers J, Said S. Double-blind, randomized, parallel group, dose-ranging study of botulinum toxin type A in the treatment of glabellar lines, Presented at the European Academy of

Dermatology and Venereology Meeting; 2001 October 10; Munich, Germany.

33) Carruthers A, Carruthers J Botulinum toxin type A for treating glabellar lines in men: a dose ranging study, Presented at the Annual Meeting of the American Academy of Dermatology; 2003 March 21-26; San Francisco, CA.

34) Ahn MS, Catten M, Maas CS: Temporal brow lift using botulinum toxin A. Reconstruct Surg 2000; 105:1129-1135.

35) Huang W, Rogachefsky AS, Foster, Brow lift with botulinumtoxin,DermatolSurg 2000; 26:55-60.

36) Huilgol SC, Carruthers A, Carruthers JDA, Raising eyebrows with botulinumtoxin,DermatolSurg 2000; 25:373-376.

37) Carruthers A, Said S. Botulinum toxin type A (BTX-A) in the treatment of glabellarrhytids: an objective analysis of treatment respons -. Presented - American Academy of Dermatology 2002 Winter Meeting; 2002 February 22-27; New Orleans, LA.

38) Carruthers A, Carruthers J- Glabella BTX-A injection and eyebrow height: a further photographic analysis. Presented- Annual Meeting

of the American Academy of Dermatology; 2003 March 21-26; San Francisco, CA.

39) Carruthers J, Carruthers A- BOTOX - in the mid and lower face and neck-SeminCutan Med Surg 2001; 20:85-92.

40) Flynn TC, Carruthers J, Carruthers A -Botulinum-A toxin treatment of the lower eyelid improves infraorbitalrhytides and widens the eye - DermatolSurg 2001; 27:703-708.

41) Armstrong MWJ, Mountain RE, Murray JAM: Treatment of facial synkinesis and facial asymmetry with botulinum toxin type A following facial nerve palsy-ClinOtolaryngol Allied Sci 1996; 21:15-22.

42) Blitzer A, Brin MF, Keen MS, Aviv JE-Botulinum toxin, for the treatment of hyperfunctional lines of the face,ArchOtolaryngol Head Neck Surg 1993; 119:1018-1022.

43) Borodic GE: Botulinum A toxin for (expressionistic) ptosis overcorrection after frontalissling,OphthalPlastReconstrSurg 1992; 8:137-142.

44) Carruthers A, Carruthers J: Clinical indications and injection technique for the cosmetic use of botulinumAexotoxin,DermatolSurg 1998; 24:1189-1194.

45) Carruthers JDA, Carruthers JA: BotulinumA exotoxin in clinical ophthalmology,CanOphthalmol 1996; 31:389-400.

46) To EW, Ahuja AT, Ho WS etalA- prospective study of the effect of botulinum toxin A, on masseteric muscle hypertrophy with ultrasonographic and electromyographic measurement. Br J PlastSurg 2001; 54:197-200.

47) von Lindern JJ, Niederhagen B, Appel T, Berge S, Reich RH - Type A botulinum toxin for the treatment of hypertrophy of the masseter and temporal muscle: an alternative treatment - PlastReconstrSurg 2001; 107:327-332.

48) Park MY, Ahn KY, Jung DS- Application of botulinum toxin A for treatment of facial contouring in the lower face. DermatolSurg 2003; 29:477-483.

49) Matarasso A, Matarasso SL, Brandt FS, Bellman B: BotulinumA exotoxin, in the management of platysma bands-PlastReconstrSurg 1999; 103:645-652.

50) Carruthers J, Carruthers A: Practical cosmetic Botox techniques, J Cutan Med Surg 1999; 3(suppl. 4):S49-S52.

51) Fagien S: Botox for the treatment of dynamic and hyperkinetic facial lines and furrows - Adjunctive use in facial aesthetic surgery. PlastReconstrSurg 2003; 112:40S-52S.

52) CarruthersJ,Zelichowska A: The power of combined therapies, Botox and ablative facial laser resurfacing - Am J CosmetSurg 2000; 17:129-131.

53) West TB, Alster TS-Effect of botulinum toxin type A,on movement-associated rhytides following CO2 laser resurfacing. DermatolSurg 1999; 25:259-261.

54) Zimbler MS, Holds JB, Kokoska MS, et al: Effect of botulinum toxin pretreatment on laser resurfacing results: a prospective, randomized, blinded trial. Arch Facial PlastSurg 2001; 3:165-169.

55) Lowe N, Lask G, Yamauchi P, Moore D, Patnaik R. Botulinum toxin type A (BTX-A) and ablative laser resurfacing (Erbium: YAG) - a comparison of efficacy and safety of combination therapy vs. ablative laser resurfacing alone for the treatment of crow's feet-Presented at the American Academy of Dermatology 2002 Summer Meeting; 2002 July 31-August 4; New York, NY.

56) Carruthers J-The effect of full-face broadband light treatments alone and in combination with bilateral crow's feet botulinum toxin type Achemodenervation. DermatolSurg 2004; 30:355.

57) Carruthers J, Carruthers A, Maberley D- Deep resting glabellarrhytides, respond to BTX-A and HylanB,DermatolSurg 2003; 29:539-544.

58) Carruthers J, Carruthers A: A prospective, randomized, parallel group study,analyzing the effect of BTX-A (Botox) and nonanimal sourced hyaluronic acid (NASHA, Restylane) in combination compared with NASHA (Restylane) alone in severe glabellarrhytides in adult female subjects: treatment of severe glabellarrhytides with a hyaluronic acid derivative compared with the derivative BTX-A-DermatolSurg 2003; 29:802-809.

59) Patel MP, Talmor M, Nolan WB: Botox and collagen for glabellar furrows: advantages of combination therapy-Ann PlastSurg 2004; 52:442-447.

60) Bushara KO, Jones JW, Park DM, Schutta HS-Botulinum toxin and sweating [abstr]-MovDisord 1995; 10:391.

61) Lowe NJ, Yamauchi PS, Lask GP, Patnaik R, Iyer S- Efficacy and safety of botulinum toxin type A in the treatment of palmar hyperhidrosis: a double-blind, randomized, placebo-controlled study-DermatolSurg 2002; 28:822-827.

62) Hurley-The eccrine sweat glands: structure and function. In: Freinkel RK, Woodley DT, ed-The Biology of the Skin, New York: Parthenon Publications; 2001:47-76.

63) Kenney LW, Munce TA: Aging and human temperature regulation-J ApplPhysiol 2003-95:2598-2603.

64) Rothman S: Sweat secretion and Biochemistry Physiology of the Skin, Chicago-Chicago University Press- 1954:162-178.

65) Sutton DR, Kowalski JW, Glaswer DA, Stang PE: US prevalence of hyperhidrosis and impact on individuals with axillary

hyperhidrosis-results from a national survey-J Am AcadDermatol 2004; 51:241-248.

66) Hornberger J, Grimes K, Naumann M, et al: Recognition, diagnosis and treatment of primary focal hyperhidrosis-J Am AcadDermatol 2004-51:274-286.

67) Hurley HJ, Shelley WB: Axillary hyperhidrosis clinical features and local surgical management-Br J Dermatol 1966; 78:127-141.

68) HigashimotoI,Yoshiura K, Hirakawa N, et al- Primary palmar hyperhidrosis locus maps to 14q11.2-q13, Am J Med Genet 2006; 140:567-572.

69) Masters W, Johnson V - Human Sexual Response, Boston: Little, Brown & Co.; 1966:287, 291.

70) Schwartzman RJ, McLellan TL: Reflex sympathetic dystrophyA review. Arch Neurol 1987; 44:555-561.

71) Linder F - Über den Einfluss der Hirnrinde auf die Schweissekretion (zurFrage der vegetativenHempilagie). Deutsche ZtschrNervenh 1947; 157:86-94.

72) Prout BJ, Wardell WM: Sweating and peripheral blood flow in patients with pheochromocytoma - ClinSci 1969; 36:109-120.

73) Sato K, Kang WH, Saga K, Sato KT - Biology of sweat glands and their disorders - Disorders of sweat gland function. J Am AcadDermatol 1999; 20:713-726.

74) Mailander JC - Heritable gustatory sweating. J Am Med Assoc 1967; 201:203-205.

75) Mellinkoff J, Mellinkoff JL - Gustatory sweating of the left knee ,J Am Med Assoc 1950; 142:901-902.

76) Bloor K: Gustatory sweating and other responses after cervico-thoracic sympathectomy. Brain 1969; 92:137-146.

77) Pasquina RF, Houston RM, Belandres PV - Beta-blockade in the treatment of autonomic dysreflexiaA case report and review, Arch Phys Med Rehab 1998; 79:582-584.

78) Hokfelt T, Johansson O, Kellerth JO, et al: Immunohistochemical distribution of substance P. In - vonEuler US, Pernow B, ed. Substance P, New York -Raven Press; 1977:117-145.

79) Randall WC: Quantitation of the output of individual sweat glands and their response to stimulation,J ApplPhysiol1949; 2:72-80.

80) LeWitt P: Hyperhidrosis and hypothermia responsive to oxybutynin,Neurology 1998; 39:506-507.

81) Edick CM: Oral glycopyrrolate for the treatment of diabetic gustatory sweating,AnnPharmacother 2005; 39:1760.

82) Torch EM: Remission of facial and scalp hyperhidrosis with clonidine hydrochloride and topical aluminum chloride. South Med J 2000; 93:68-69.

83) Manusov EG, Nadeau MT: Hyperhidrosis: a management dilemma. J FamPract 1989; 28:412-415.

84) Connolly M, de Berker D: Management of primary hyperhidrosis: a summary of the different treatment modalities - Am J ClinDermatol 2003; 4:861-897.

INRODUCTION

AIM OF THE STUDY

REVIEW OF LITERATURE

MATERIALS AND METHODS

RESULTS

DISCUSSION

CONCLUSION

BIBLIOGRAPHY

ANNEXURES

PROFORMA

Name Age Sex

Skin O.P No:

Occupation:

Address:

Per capita income:

Presenting complaints:

H/O present illness :

- Onset
- Duration
- Course
- H/O associated symptoms
- H/O predisposing factors
- H/O aggravating/relieving factors
- H/O abdominal distension/mass/pain
- H/O other systemic disturbances

Past history:

H/O any major medical/surgical illness

Family history:

Personal history:

Diet:

Sleep:

Appetite:

Bowel & bladder habits:

Habits: smoking/alcoholism

Menstrual history (in females):

Menarche/menopause; cycles; flow

Obstetric history (in females):

H/O pregnancy/lactation

Treatment history:

H/O previous treatment / surgeries

H/O allergy to botox

General physical examination:

Consciousness; orientation

Built & nourishment

Febrile/afebrile

Pallor/cyanosis/clubbing/icterus/lymphadenopathy/pedal edema

Pulse rate: Peripheral pulses:

Blood pressure:

Respiratory rate:

Temperature:

Systemic examination:

Cardiovascular system:

Respiratory system:

Abdomen:

Central nervous system:

Local examination:

I HYPERHIDROSIS:

Inspection – sites of involvement , skin over the sites

II WRINKLES:

Inspection – sites involved, type of wrinkles , skin over the face

Clinical test –

Minors starch iodine test – assess and document severity

Hyperhidrosis severity score system – subjective assessment

Photographic recording – pre & post procedure

DIAGNOSIS:

INVESTIGATIONS:

Hb%, TC, DC, ESR , Platelet

Urine – albumin, sugar, deposits

BT, CT

Thyroid profile

BOTOULINUM TOXIN VIAL

PROCEDURE TRAY

DURING PROCEDURE - HYPERHIDROSIS

DURING PROCEDURE - WRINKLES

PALMAR HYPERHIDROSISBEFORE TREATMENT

RIGHT HAND TO BE TREATED

COMPLETE RESPONSE AFTER TREATMENT

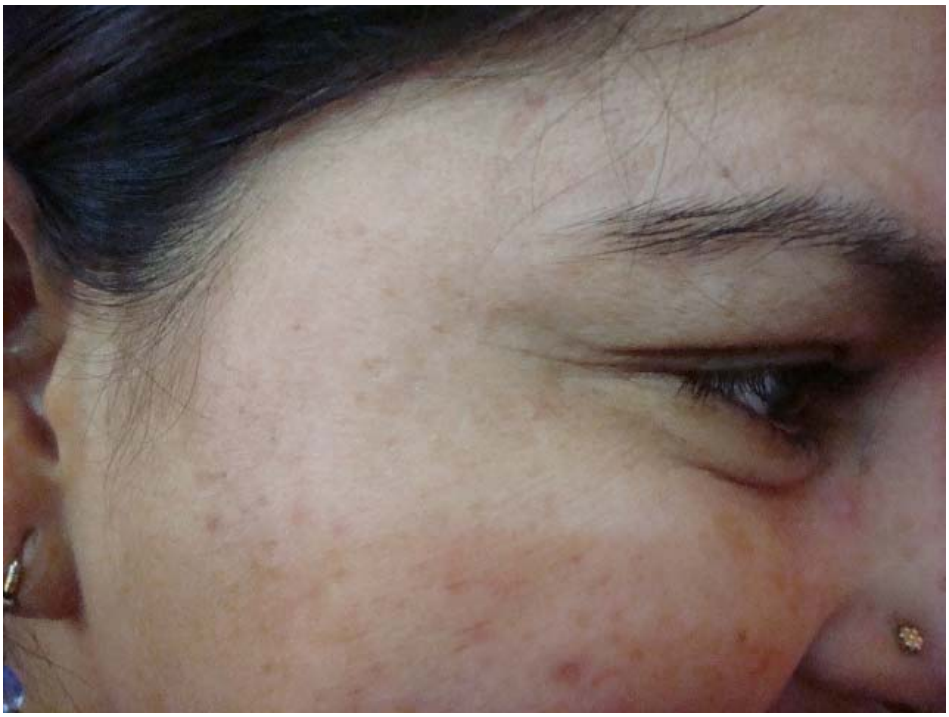
PALMAR HYPERHIDROSISBEFORE TREATMENT

LEFTHAND TO BE TREATED

PARTIAL RESPONSE AFTER TREATMENT

CROWS FEET – BEFORE TREATMENT

COMPLETE RESPONSE AFTER TREATMENT



CROWS FEET – BEFORE TREATMENT

COMPLETE RESPONSE AFTER TREATMENT

CROWS FEET – BEFORE TREATMENT

COMPLETE RESPONSE AFTER TREATMENT

CROWS FEET – BEFORE TREATMENT

COMPLETE RESPONSE AFTER TREATMENT

CROWS FEET – BEFORE TREATMENT

PARTIAL RESPONSE AFTER TREATMENT

MARKING FOR FOREHEAD WRINKLES

IMMEDIATE POST PROCEDURE

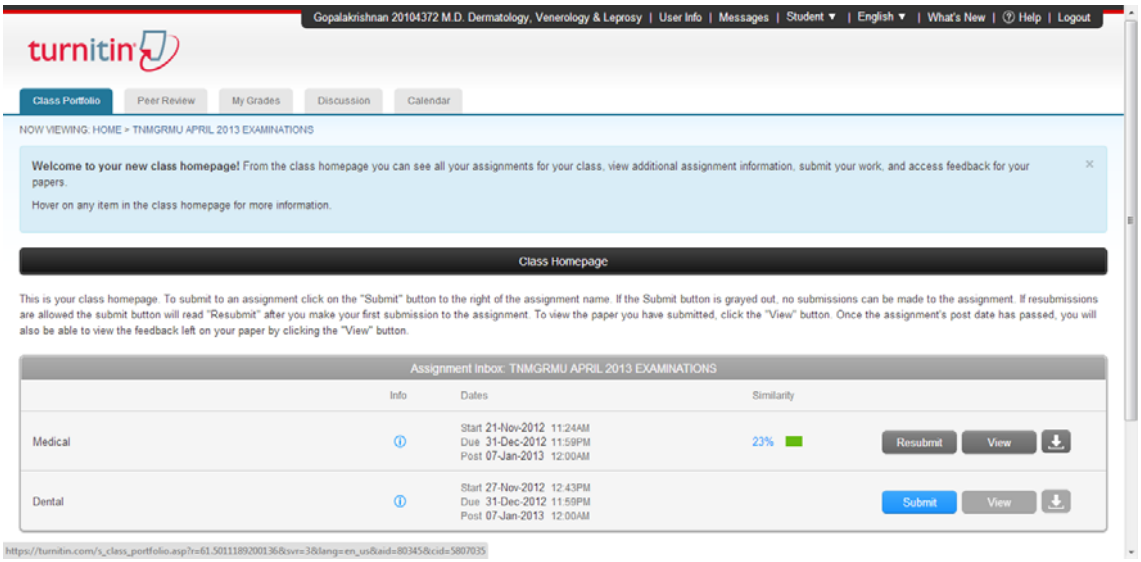
COMPLICATION - HEMATOMA

MASTER CHART – HYPERHIDROSIS

S.NO	NAME	AGE	SEX	HEMOGRAM	BT	CT	THYROID PROFILE	REPSONSE TO TREATMENT	OVERALL SATISFACTION WITH TREATMENT
1.	MURALI	32	M	WNL	2’ 10’’	4’ 27’’	WNL	COMPLETE	GOOD
2.	KARTHIK	29	M	WNL	3’ 06’’	5’ 01’’	WNL	COMPLETE	GOOD
3.	SHALINI	18	F	WNL	2’ 12’’	6’ 11’’	WNL	COMPLETE	GOOD
4.	MALAR	26	F	WNL	2’ 16’’	4’ 31’’	WNL	PARTIAL	FAIR
5.	ESTHER	35	F	WNL	3’ 10’’	4’ 43’’	WNL	COMPLETE	GOOD
6.	MARIAMMA	27	F	WNL	4’ 00’’	4’ 34’’	WNL	COMPLETE	GOOD
7.	KANCHANA	19	F	WNL	2’ 17’’	5’ 21’’	WNL	COMPLETE	GOOD
8.	MARY	22	F	WNL	2’ 07’’	6’ 17’’	WNL	COMPLETE	GOOD
9.	RAVI	38	M	WNL	2’ 14’’	4’ 11’’	WNL	COMPLETE	GOOD
10.	MANIMEGALAI	25	F	WNL	3’ 18’’	4’ 23’’	WNL	COMPLETE	GOOD
11.	RANI	21	F	WNL	4’ 02’’	4’ 45’’	WNL	COMPLETE	GOOD
12.	SHOBANA	22	F	WNL	3’ 15’’	5’ 29’’	WNL	COMPLETE	GOOD
13.	NITHYA	20	F	WNL	2’ 19’’	4’ 11’’	WNL	PARTIAL	FAIR
14.	POOJA	19	F	WNL	2’ 34’’	5’ 21’’	WNL	COMPLETE	GOOD
15.	SHANKAR	19	M	WNL	2’ 17’’	4’ 35’’	WNL	COMPLETE	GOOD
16.	SENTHAMIL	29	F	WNL	3’ 10’’	4’ 23’’	WNL	COMPLETE	GOOD
17.	SELVI	22	F	WNL	4’ 19’’	6’ 00’’	WNL	COMPLETE	GOOD
18.	VALAVAN	23	M	WNL	2’ 13’’	4’ 20’’	WNL	COMPLETE	GOOD
19.	ERUSAMMA	31	F	WNL	2’ 15’’	4’ 15’’	WNL	COMPLETE	GOOD
20.	CHITRA	41	F	WNL	2’ 15’’	5’ 11’’	WNL	COMPLETE	GOOD

MASTER CHART – WRINKLES

S.NO	NAME	AGE	SEX	HEMOGRAM	BT	CT	REPSONSE TO TREATMENT	OVERALL SATISFACTION WITH TREATMENT
1.	SANDHYA	32	F	WNL	2’ 10’’	4’ 27’’	COMPLETE	GOOD
2.	MANI	29	M	WNL	3’ 06’’	5’ 01’’	COMPLETE	GOOD
3.	SHARADHA	55	F	WNL	2’ 12’’	6’ 11’’	COMPLETE	GOOD
4.	LEELA	26	F	WNL	2’ 16’’	4’ 31’’	PARTIAL	FAIR
5.	SHANKARI	35	F	WNL	3’ 10’’	4’ 43’’	COMPLETE	GOOD
6.	YOGESHWARI	27	F	WNL	4’ 00’’	4’ 34’’	COMPLETE	GOOD
7.	THARANI	39	F	WNL	2’ 17’’	5’ 21’’	COMPLETE	GOOD
8.	POORANI	59	F	WNL	2’ 07’’	6’ 17’’	COMPLETE	GOOD
9.	BABA	38	M	WNL	2’ 14’’	4’ 11’’	COMPLETE	GOOD
10.	HARINI	35	F	WNL	3’ 18’’	4’ 23’’	COMPLETE	GOOD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